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09/747,760	12/21/2000	Richard Glynne	18547-046600US	4702

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EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	

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18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/747,760	Mack et al
Examiner	**Art Unit**
Padmashri Ponnaluri	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 19, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 22-35* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 22-35* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CAR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CAR 1.114, and the fee set forth in 37 CAR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CAR 1.114. Applicant's submission filed on 8/19/03 has been entered.

2. This application claims priority to provisional application 60/171,796 filed on 12/22/99.

3. The amendment B, filed on 8/19/03 has been fully considered and entered into the application.

4. Claims 2-21 have been canceled and new claims 22-35 have been added by the amendment B, filed on 8/19/03. Claims 1, 22-35 are currently pending and are being examined in this application.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (i.e., see page 12, line 11). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material

incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 U. S. P. Q. 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 U. S. P. Q. 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 U. S. P. Q. 167 (CCPA 1973).

7. The attempt to incorporate subject matter into this application by reference to PCT applications (i.e., see pages 19, 37) is improper because the subject matter disclosed in the PCT applications is important to practice the current invention.

8. The use of the trademark (AFFYMETRIX GENE CHIP ARRAY in page 77) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Applicants are requested to check the entire specification and correct all the Trade names and should be capitalized.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

9. The listing of references in the specification is not a proper information disclosure statement. 37 CAR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

10. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The newly added limitations 'providing a cell' and 'as a potential immunosuppressant' claimed in claim 1 has no clear support in the specification and the claims as originally filed. The specification discloses the use of B cells that express one or more expression profile genes in the method for screening for a drug candidate. The specification does not disclose the use of any other cell. The subject matter claimed in claim 1 broadens the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

13. Claims 1, 22-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims briefly recite a method of screening drug candidates by adding a drug candidate to a cell that expresses expression profile genes, and determining the effect of the drug candidate on the expression of the expression profile of the gene. And further the claims recite that the identified drug candidate is a 'potential immunosuppressant or B cell modulator or B cell tolerance' are considered as intended or inherent property of the identified compounds.

The instant specification discloses a method for screening for a drug candidate using specific genes as markers which are presented on a gene chip. The specification has discloses the use of a known immunosuppressant FK 506 (drug candidate) to screen an array of genes to identify the expression of the genes in B cells. Th specification has not disclosed the use of the claimed method in identifying any other drug and then determine the identified drug as an immunosuppressant or B cell modulator.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405

(1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

This holding would be deemed to be applicable to the claimed method because the specification has not disclosed that using the claimed method that the drug candidate identified is a immunosuppressant or B cell modulator. The specification uses a known immunosuppressant as drug to identify different gene expressions or comparison of gene expression in B cells. The specification has not identified compounds or drugs identified by the claimed method are immunosuppressants or B cell modulators The specification has no examples of compounds identified by the claimed method as immunosuppressants or B cell modulators. The specification disclosure at the time of filing of the invention requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding the potential immunosuppressants or B cell modulators identified by the claimed method.

Additionally, the narrow scope of examples directed to the use of known immunosuppressant FK506 are clearly not representative of the scope of the presently claimed invention..

14.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1, 22-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite ' potential immunosuppressant' or 'potential modulator', or ' B cell tolerance' in which the term 'potential' is considered as 'capable of being and not yet existing'. Thus, the drug or the compound identified by the reference method is not yet identified or confirmed as a potential modulator of B cells or potential immunosuppressant.

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1, 22-23, 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by . Foulkes et al (US Patent 5,580,722).

The instant claims briefly recite a method of screening drug candidates by adding a drug candidate to a cell that expresses expression profile genes, and determining the effect of the drug

candidate on the expression of the expression profile of the gene. NOTE that the 'potential immunosuppressant or B cell modulator or B cell tolerance' are considered as intended or inherent property of the identified compounds.

Foulkes et al disclose a method to determine whether a molecule not previously known to be a modulator of protein biosynthesis is capable of directly and specifically transcriptionally modulating the expression of a gene encoding a protein of interest associated with treatment of one or more symptoms of a cardiovascular disease (i.e., see abstract). The reference discloses that the cardiovascular disease may be associated with thrombosis (i.e., see column 21). The reference discloses that the protein of interest may be CD36 (i.e., see column 21, line 66) (refers to one of expression profile gene of the instant claims). The reference discloses in claim 1, a method of determining whether a chemical not previously known to be modulator of protein biosynthesis (refers to drug candidate of the instant claims) is capable of modulating expression of a gene encoding a protein of interest, by contacting the sample which contains the predefined eukaryotic cells consisting of gene encoding protein of interest (refers to the cell of the instant claims); quantitatively determining the amount of the signal so produced (refers to step c) of the instant claims); comparing the amount so determined with the amount of produced signal detected in the absence of any chemical being tested refers to instant claim step d)). Foulkes et al do not teach the compound or molecule identified by the claimed method is a **potential modulator of B cells or B cell tolerance or potential immunosuppressant**. However, the reference teaches the gene encoding the protein of interest is associated with cardiovascular disease and thrombosis and the

protein is CD36 (refers to the one of the expression profile gene of the instant claims). CD36 is also known as gp IV or gp IIIb and found on monocytes, macrophages, platelets and on B cells. Thus, the tested molecule is a modulator of a protein interest (CD 36), which is considered as a potential modulator of B cell or immunosuppressant. Thus the reference clearly anticipates the claimed invention.

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1, 22-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/10365 (LOCKHART et al) and Grosveld et al (US Patent 6,110,666) .

The instant claims briefly recite a method of screening drug candidates by adding a drug candidate to a cell that expresses expression profile genes, and determining the effect of the drug candidate on the expression of the expression profile of the gene. NOTE that the 'potential immunosuppressant or B cell modulator or B cell tolerance' are considered as intended or inherent property of the identified compounds.

Lockhart et al teach methods of monitoring the expression levels of a multiplicity genes. The reference teaches a method of identifying genes that are effected by one or more dugs, or conversely screening a number of drugs to identify those that have effect on particular genes (i.e., see page 8, lines 31-32 and the line bridging pages 8 and 9). The method provides a pool of target nucleic acids from one or more cells (refers to the instant clams steps a) and b)) contacted with the drug or drugs and hybridizing that pool to any of the high density oligonucleotide arrays. The reference teaches that the expression levels of the genes targeted by the probes in the array are determined and compared to expression levels of genes from control cells not exposed to the drug or drugs (refers to instant claim step d)) (i.e., see page 9, lines 1-6). The genes that are over expressed or under expressed in response to the drugs are identified or conversely the drug or drugs that alter expression of one or more genes is identified (i.e., see page 9, lines 6-8).

The reference teaches that the genes of particular interest for expression monitoring include genes involved in pathways associated with various pathological conditions (e.g., cancer) and whose expression is thus indicative of the pathological condition. Such genes include but are

not limited to HER2 (c-erbB-2/neu), receptor protein kinases associated with etiologiy of number of tumors including carcinomas of breast, liver, bladder, pancreas as well as glioblastomas, sarcomas, squamous carcinomas, tumor suppressor genes such as p53 and other marker genes such as RAS, MSH2, MLH1, BRCA1. Other genes of particular interest for expression monitoring are genes involved in the immune responses, as well genes involved in cell adhesion and signal transduction, etc. (I.E., see page 8, lines 19-29).

The claimed invention differs from the prior art teachings by reciting specific cells that express specific genes . Lockhart et al teaches a method of identifying genes that are effected by one or more dugs. The reference teaches that the genes of particular interest for expression monitoring include genes involved in pathways associated with various pathological conditions, and genes involved in immune responses, cell adhesion and signal transduction. The reference does not teach cells that expression of specific gene markers as in the instant claims. However, Grosveld et al (US Patent 6,110,666) teaches pre-B cell possess CD72 as cellular marker gene (i.e., see column 8, lines 8-9). The reference teaches a composition for targeted gene delivery to a target cell composing immune cell surface antigen CD72 (i.e., see column 22, lines 65-66). The reference teaches monitoring the levels of transduction, gene expression and/or the presence or levels of normal encoded protein will assist in selecting and adjusting the dosage administered (i.e., see column 23, lines 34-36).

Thus it would have been obvious to one skilled in the art at the time the invention was made to use the cells that express CD72 gene taught by Grosveld et al in the drug screening

methods, because Lockhart et al teach a method of identifying genes that are effected by one or more dugs, Lockhart et al teaches that the genes of particular interest for expression monitoring include genes involved in pathways associated with various pathological conditions, genes involved in immune response.

20. No claims are allowed.

21. Applicant's arguments with respect to claims 1-2 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
17 November 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER